Scientific Abstract

BRCA1 may be responsible for both hereditary and sporadic breast and ovarian cancer. The hereditary form is usually from a mutation combined with the loss of heterozygosity of the BRCA1 gene, which our gene therapy would replace. The sporadic forms are usually from a decreased BRCA1 expression presumably due to BRCA1 promoter methylation. Our gene therapy would administer the full length BRCA1 gene to the patient via a retrovirus. By taking advantage of the fact that retroviruses preferentially infect dividing cells, this would deliver our gene therapy where it is needed most, i.e., the rapidly dividing cancer cells. The purpose of this study is to use a retrovirus to transduce ovarian cancer cells with the full length BRCA1 gene and evaluate the effect on tumor growth in patients.

Experiments in mice have shown that the transfer of BRCA1 gene into cancer cells using a retroviral vector results in a striking reduction in growth of cancer. In a preliminary phase I study of retroviral BRCA1 gene therapy in patients with metastatic ovarian cancer, we evaluated dosing, toxicity, and response to treatment. We found toxicity was minimal, particularly when compared to cytotoxic chemotherapy, and one patient demonstrated a measurable response. Based on these findings, we performed a partial phase II which was halted because of the instability of vector and lack of benefit found in the healthier phase II patients. We propose a phase I/II clinical trial with our new complement resistant retroviral vector (MFG-BRCA1). Patients will undergo intraperitoneal infusion of retroviral BRCA1 therapy. Eligible patients will be those who have completed first-line surgery and chemotherapy and are candidates for second- look surgery or have recurrent disease and have measurable disease < 3cm.